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**APPENDIX A - SPECIFICATION/CLAIM AMENDMENTS
INCLUDING NOTATIONS TO INDICATE CHANGES MADE**

Serial No.: 09/727,739

Docket No.: 255.00040101

Amendments to the following are indicated by underlining what has been added and bracketing what has been deleted. Additionally, all amendments have been shaded.

In the Specification

The paragraph beginning at **page 11, line 7**, has been amended as follows:

Trout preprosomatostatin-II" (PPSS-II") is described herein in Example III and is shown in Fig. 1 and Fig. 3. PPSS-II" is characterized by a 600 base pair cDNA (SEQ ID NO:20) that encodes a precursor protein of about 111 amino acids (SEQ ID NO:15) that appears capable of being processed into a 25 amino acid polypeptide (SEQ ID NO:16), and further into a 14 amino acid peptide (SEQ ID NO:12). Because this tetradecapeptide has the modified [Tyr⁷, Gly¹⁰] sequence, these somatostatins are members of the SS-II family.

The paragraph beginning at **page 12, line 22**, has been amended as follows:

Percent identity is determined by aligning the residues of the two amino acid or nucleotide sequences to optimize the number of identical amino acids or nucleotides along the lengths of their sequences; gaps in either or both sequences are permitted in making the alignment in order to optimize the number of identical amino acids or nucleotides, although the amino acids or nucleotides in each sequence must nonetheless remain in their proper order. Preferably, two amino acid sequences are compared using the Blastp program, version 2.0.9, of the BLAST 2 search algorithm, as described by [Fatana J. Tansova, et al. (*FEMS Microbiol. Lett.*, 174, 247-250 (1999)), and available on the world wide web at <http://www.ncbi.nlm.nih.gov/blast.html>. Preferably, the default values for all BLAST 2 search parameters are used, including matrix = BLOSUM62; open gap penalty = 11, extension gap penalty = 1, gap x_dropoff = 50, expect = 10, wordsize = 3, and filter on. Likewise, two nucleotide sequences are compared using the Blastn program, version 2.0.11, of the BLAST 2 search algorithm, also as described by [Fatana J. Tansova, et al. (*FEMS Microbiol. Lett.*, 174, 247-250 (1999)), and available on the world wide web at <http://www.ncbi.nlm.nih.gov/blast.html>.

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www.ncbi.nlm.nih.gov/blast.html. Preferably, the default values for all BLAST 2 search parameters are used, including reward for match = 1, penalty for mismatch = -2, open gap penalty = 5, extension gap penalty = 2, gap x_dropoff = 50, expect = 10, wordsize = 11, and filter on.

The paragraph beginning at **page 14, line 31**, has been amended as follows:

Further, the single-stranded polynucleotide of the invention also includes a polynucleotide fragment having a nucleotide sequence that is substantially complementary to (a) a nucleotide sequence that encodes a novel somatostatin polypeptide according to the invention, or (b) the complement of such nucleotide sequence. "Substantially complementary" polynucleotide fragments can include at least one base pair mismatch, such that at least one nucleotide present on a second polynucleotide fragment, however the two polynucleotide fragments will still have the capacity to hybridize. For instance, the middle nucleotide of each of the two DNA fragments 5'-AGCAAATAT and 5'-ATATATGCT will not base pair, but these two polynucleotide fragments are nonetheless substantially complementary as defined herein. Two polynucleotide fragments are substantially complementary if they hybridize under hybridization conditions exemplified by 2X SSC (SSC: 150mM NaCl, 15 mM trisodium citrate, pH 7.6) at 55°C. Substantially complementary polynucleotide fragments for purposes of the present invention preferably share at least one region of at least 20 nucleotides in length which shared region has at least 60% nucleotide identity, preferably at least 80% nucleotide identity, more preferably at least 90% nucleotide identity and most preferably at least 95% nucleotide identity. Particularly preferred substantially complementary polynucleotide fragments share a plurality of such regions. Locations and levels of nucleotide sequence identity between two nucleotide sequences can be readily determined using CLUSTALW multiple sequence alignment software (J. Thompson et al., *Nucleic Acids Res.*, 22:4673-4680 (1994)), available on the world wide web at <http://www.ebi.ac.uk/clustalw/>.

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In the Claims

For convenience, all pending claims are shown below.

1. (Amended) A antisense or purified somatostatin polypeptide or bioactive analog comprising a polypeptide selected from the group consisting of:
 - (a) a polypeptide comprising SEQ ID NO 15;
 - (b) a subunit thereof of the polypeptide of (a) comprising SEQ ID NO 16 and at least 7 contiguous amino acids from SEQ ID NO 17;
 - (c) an analog of the polypeptide of (a) that has an amino acid sequence at least about 85% identical to SEQ ID NO 15; and
 - (d) an analog of the subunit of (b) having an amino acid sequence at least about 90% identical to the amino acid sequence of the subunit of the somatostatin polypeptide comprising at least one amino acid sequence comprising at least one of a portion of *Oncorhynchus mykiss* preprosomatostatin I (PPSS-I, SEQ ID NO 2) and a portion of *Oncorhynchus mykiss* preprosomatostatin II (PPSS-II, SEQ ID NO 15);
 wherein the somatostatin polypeptide binds to a somatostatin receptor.
2. (Amended) The somatostatin polypeptide or bioactive analog or subunit thereof of claim 1, wherein the somatostatin polypeptide comprises at least one amino acid sequence selected from the group consisting of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 9, 10, 11, 12, 13, 15, 16, 17, 18, and 19.
3. (Amended) A polypeptide comprising at least one amino acid sequence selected from the group consisting of SEQ ID NOs: 3, 4, 5, 6, 7, 9, 10, 11, 12, 13, 15, 17, 18, and 19.
4. (Amended) A polynucleotide comprising at least one nucleotide sequence that encodes at least one somatostatin polypeptide or bioactive analog or subunit thereof of claim 1.

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5. (Amended) The polynucleotide of claim 4 comprising ~~SEQ ID NO: 3~~ SEQ ID NO:20.
6. A polynucleotide that is substantially complementary to the polynucleotide of claim 4.
7. A method for identifying a modified somatostatin polypeptide comprising:
 - (a) providing an amino acid sequence of a somatostatin polypeptide comprising at least one amino acid sequence selected from the group consisting of SEQ ID NOs:3, 4, 5, 6, 7, 9, 10, 11, 12, 13, 15, 17, 18, and 19;
 - (b) aligning the amino acid sequence of the somatostatin polypeptide of step(a) with the amino acid sequence of a reference somatostatin polypeptide;
 - (c) identifying at least one site or region of differing amino acid sequence; and
 - (d) modifying the amino acid sequence of the somatostatin polypeptide of step (a) or the reference somatostatin polypeptide at the identified site or region to incorporate at least one amino acid substitution, insertion, or deletion from the analogous site or region in the other somatostatin polypeptide to yield the amino acid sequence of a modified somatostatin polypeptide.
8. The method of claim 7 further comprising (e) synthesizing the modified somatostatin polypeptide and (f) assaying the modified somatostatin polypeptide for biological activity.
9. The method of claim 8 wherein step (e) comprises assaying the binding of the modified somatostatin polypeptide to a human somatostatin receptor.
10. The method of claim 7 wherein the reference somatostatin polypeptide is a mammalian somatostatin polypeptide.

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11. The method of claim 7 wherein the modified somatostatin polypeptide is a somatostatin agonist or antagonist.
12. (Amended) A fusion polypeptide comprising an N-terminal somatostatin region comprising at least one first amino acid sequence comprising a somatostatin polypeptide or a fragment of a portion of *O. mupis* preprosomatostatin I (PPSS-I, SEQ ID NO:3) and a portion of *O. mupis* preprosomatostatin II (PPSS-II, SEQ ID NO:5) covalently linked to a C-terminal region comprising a second amino acid sequence.
13. The fusion polypeptide of claim 12 wherein the second amino acid sequence encodes a bioactive moiety.
14. (Amended) The fusion polypeptide of claim 12 wherein the first amino acid sequence comprises at least one amino acid sequence selected from the group consisting of NOs: 1, 4, 5, 6, 7, 9, 10, 11, 12, 13, 15, 16, 17, 18, and 19.
15. (Amended) The fusion polypeptide of claim 13 wherein the first amino acid sequence comprises SEQ ID NO:6 or SEQ ID NO:18.
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